

Integrating Genetic and Clinical Information for Treatment Decision-Making in Women With Breast Cancer

Burke, Harry B.¹, Weitzel, Jeffrey N.², Narod, Stephen A.³

¹George Washington University School of Medicine, Washington, DC, USA; ²City of Hope, Duarte, CA, USA; ³University of Toronto, Canada

Background: It is critical to know how to use genomic information to help physicians and patients make informed treatment decisions. For women with breast cancer who are BRCA positive, we have developed a clinical decision making tool that integrates genetic and clinical information and provides the clinician and patient with the patient's individual risk of contralateral breast cancer (a second primary tumor) and of disease-specific survival.

Methods: The data set was a multi-institutional collaboration of 1,139 women with breast cancer who were BRCA positive. Women were included if they were less than 66 years of age, were diagnosed with Stage I or Stage II breast cancer, and were either BRCA1 or BRCA2 positive. 647 women were alive and 492 were deceased. SAS (Cary, NC) was used to construct proportional hazards models for risk of contralateral breast cancer and of disease-specific survival. The area under the receiver operating characteristic (ROC) was used to assess model accuracy. Visual Basic (Microsoft Corp., Redmond, WA) was used to construct a visual interface for data entry and for the underlying algorithm. ACCESS (Microsoft, Redmond, WA) was used for the data base.

Results: We created an algorithm that integrates the patient's clinical and genetic information and provides as its output the patient's individual probability of contralateral breast cancer and death due to breast cancer (shown below). The model inputs are age at diagnosis, BRCA1 or BRCA2, ER and PR status, lymph node involvement, tumor size, and type of primary surgery. The outputs are the relative risk, five-year and ten-year probability of contralateral breast cancer and of disease-specific survival for tamoxifen, chemotherapy, prophylactic mastectomy, and prophylactic oophorectomy.

The screenshot shows the BRCA1x software interface. It has a menu bar (File, Edit, View, Help) and a toolbar. The main window is divided into several sections:

- PATIENT INFORMATION:** Fields for Name, Address, Address 2, Phone, EOB, Date, and Country.
- BREAST CANCER INFORMATION:** Fields for BC (Breast Cancer) and OC (Ovarian Cancer) status, and checkboxes for Mother, Sister 1, Sister 2, Sister 3, Aunt 1, Daughter 1, and Daughter 2.
- FAMILY HISTORY INFORMATION:** Fields for Age, BRCA1, BRCA2, ER, PR, Post Nodes, Tumor Size, and Surgery.
- Buttons:** Calculate, Add, and Delete.
- Table:** A table showing calculated risks for Contralateral Breast Cancer and Breast Cancer survival. The table has columns for Tamoxifen, Chemo, Rad, Prophy, Oopho, Rel-Risk, 5 Yr-Risk, 10Yr-Risk, and 5 Yr-Risk. The table contains 10 rows of data.

Conclusion: This tool is being used to help patients make informed treatment decisions. It is a model of how to integrate genetic information into the practice of medicine.